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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,464	03/28/2001	Martin Friede	B45070-1	1150

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT PAPER NUMBER

1648

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/819,464	Applicant(s) FRIEDE ET AL.	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 74-94 is/are pending in the application.
- 4a) Of the above claim(s) 85-93 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 74-84 and 94 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 74-94 are currently pending in the application.
2. In the prior action, claims 94-93 were pending, with claims 74-84 rejected, and claims 85-93 withdrawn as to non-elected inventions. In the Response of February 9, 2006, the Applicant amended claims 74 and 75, and added new claim 94.

Claims 74-84 and 94 are under consideration.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. **(Prior Rejection- Maintained)** Claims 74-76, 78, 80, and 82-84 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lipford in view of the teachings of Kensil. These claims describe compositions comprising an antigen, the saponin QS-21, and sterol (preferably cholesterol) in excess by weight to the saponin of 1:2 to 1:100. Newly added claim 93 additionally requires that the composition is in the form of a unilamellar liposome. As such compositions are suggested by Lipford, the rejection is extended to this claim.

The teachings of Lipford and Kensil have been described previously. The Lipford reference teaches the formation of Quil A containing liposomes as an alternative to the use of ISCOMs because liposomes are more versatile with respect to the incorporation and delivery of antigens. Page 78. Kensil teaches that the QS21 fraction of Quil A has adjuvant properties. Thus,

Art Unit: 1648

it would have been obvious to those in the art to substitute this purified fraction for the crude Quil A used in Lipford.

In the Response, the Applicant traverses the rejection on two grounds. First, the Applicant asserts that the art teaches that QS21 is not able to form ISCOMs, and that those in the art would therefore not be motivated to combine the teachings of Lipford with those of Kensil. Second, the Applicant asserts that there would be insufficient motivation to use QS21 in the place of Quil A as the Kensil reference does not clearly teach that the fraction has either greater adjuvant effect or lower hemolysis than Quil A. These arguments are not found persuasive.

With respect to the first argument, it is noted that the present claims are not drawn to the incorporation of QS21 into ISCOMs. Rather, the application specifically teaches that the presently claimed compositions, wherein the sterol is in excess to the saponin, are liposomes; whereas in ISCOMs the saponin is present in excess of the sterol. See e.g., pages 5 and 9. Further, Lipford is teaching liposomes as an alternative to the use of ISCOMs. While the properties of ISCOMs were referred to in the prior action, this was to show indications of adjuvant effect, and not as an indication as to the structure suggested by the references. Thus, the fact that QS21 may not have been known in the art to form ISCOMs does not tech away from its incorporation into liposomes.

In addition, it is noted that one of the two references relied on by the Applicant to show that QS21 does not form ISCOMs per se, does teach that QS21 binds to and forms an ISCOM-like complex with cholesterol. WO 92/06710, pages 18-19. Thus, while those in the art may not have had a reasonable expectation of success in the use of QS21 containing ISCOMs, they would have had sufficient information to suggest that the saponin could be incorporated into liposomal

Art Unit: 1648

formations with cholesterol as suggested by Lipford. It is additionally noted that Kensil also indicates that the saponins disclosed therein may be incorporated into liposomes. See e.g., column 11, lines 27-29. See also, Prieels et al., WO 94/00153, pages 5-6 (suggesting the incorporation of an adjuvant composition comprising QS21 into a carrier, such as a liposome). Thus, the teachings of the art regarding the lack of ISCOM formation using QS21 are not sufficient to demonstrate that the saponin would not have been expected to work in a liposomal formation such as in Lipford.

With respect to the suggestion for the use of QS21 in Kensil, regardless of the teachings in Kensil regarding the operability of QS21 in comparison to Quil A, the reference does indicate that the compound has adjuvant activity. Thus, because the art indicates that both Quil A and QS21 are adjuvants (Kensil, column 6) and are thus functional equivalents, it would have been prima facie obvious to substitute one with the other. See e.g., MPEP § 2144.06. Thus, the Applicant's arguments with respect to the suggestion for the substitution of QS21 for Quil A are also not found persuasive.

For these reasons, and the reasons of record, the rejection is maintained.

5. **(Prior Rejection- Maintained)** Claims 77, 79, and 81 were additionally rejected under 35 U.S.C. 103(a) as being unpatentable over either Lipford in view of Kensil as applied against claims 74-76, 78, 80, 82-84, and 94 above, and further in view of Prieels et al. (WO 94/00153). Dependent claims 77, 79, and 81 describe a composition as claimed above wherein the adjuvant formulation also comprises alum salts and/or 3 De-O-acylated monophosphoryl lipid A. The

Art Unit: 1648

Applicant traverses this on the same grounds as argued with respect to the rejection over Lipford and Kensil above.

In addition to the teachings of Lipford and Kensil, the Prieels reference provides additional motivation to use the QS21 formulation disclosed therein to take advantage of the synergy of this Quil A fraction with 3D-MPL, or 3D-MPL and an aluminum salt. Further, as was indicated above, this reference also specifically indicates that the compositions may be delivered in the form of a liposome. Pages 5-6. These teachings, in combination with those of Lipford teaching the added benefits for the use of liposomes in saponin adjuvant formulations, would have rendered the claimed compositions obvious to those of ordinary skill in the art. Thus, for these reasons, and the reasons described above, the Applicant's arguments in traversal are not found persuasive.

Conclusion

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

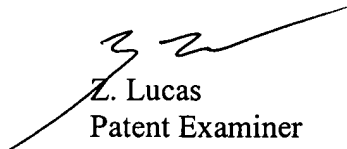
Art Unit: 1648

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

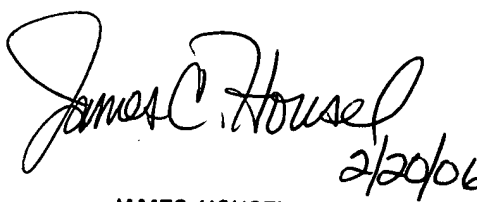
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Z. Lucas
Patent Examiner



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